DEPARTMENT OF THE AIR FORCE
59TH MEDICAL WING (AETC)
JOINT BASE SAN ANTONIO - LACKLAND TEXAS

15 APR 2016

MEMORANDUM FOR SGOZ
ATTN: CAPT NATHANIEL S NYE

FROM: 59 MDW/SGVU

SUBJECT: Professional Presentation Approval

1. Your paper, entitled **Improving Stress Fractures Diagnosis: Algorithm and Clinical Prediction Rule** presented at **American Medical Society for Sports Medicine, Texas, 16-20 April 2016** with MDWI 41-108, and has been assigned local file #**16150.**

2. Pertinent biographic information (name of author(s), title, etc.) has been entered into our computer file. Please advise us (by phone or mail) that your presentation was given. At that time, we will need the date (month, day and year) along with the location of your presentation. It is important to update this information so that we can provide quality support for you, your department, and the Medical Center commander. This information is used to document the scholarly activities of our professional staff and students, which is an essential component of Wilford Hall Ambulatory Surgical Center (WHASC) internship and residency programs.

3. Please know that if you are a Graduate Health Sciences Education student and your department has told you they cannot fund your publication, the 59th Clinical Research Division may pay for your basic journal publishing charges (to include costs for tables and black and white photos). We cannot pay for reprints. If you are 59 MDW staff member, we can forward your request for funds to the designated wing POC.

4. Congratulations, and thank you for your efforts and time. Your contributions are vital to the medical mission. We look forward to assisting you in your future publication/presentation efforts.

Linda Steel-Goodwin

LINDA STEEL-GOODWIN, Col, USAF, BSC
Director, Clinical Investigations & Research Support

PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

1. TO: CLINICAL RESEARCH	2. FROM: (Author's Name, Rank, Grade, Office Symbol)	3. GME/GHSE STUDENT:	4. PROTOCOL NUMBER:
	Nathaniel S. Nye, Capt, USAF, MC, 559 THLS/SGOZ	☐ YES ☒ NO	FWH20150083N

5. PROTOCOL TITLE: (**NOTE:** For each new release of medical research or technical information as a publication/presentation, a new 59 MDW Form 3039 must be submitted for review and approval.)

Evaluating an Algorithm and Clinical Prediction Rule to Improve Diagnostic Accuracy and Management of Pelvic and Lower Extremity Bone

6. TITLE OF MATERIAL TO BE PUBLISHED OR PRESENTED:

Improving Stress Fracture Diagnosis: Algorithm and Clinical Prediction Rule

7. FUNDING RECEIVED FOR THIS STUDY? ☐ YES ☒ NO FUNDING SOURCE:

8. DO YOU NEED FUNDING SUPPORT FOR PUBLICATION PURPOSES: ☐ YES ☒ NO

9. IS THIS MATERIAL CLASSIFIED? ☐ YES ☒ NO

10. IS THIS MATERIAL SUBJECT TO ANY LEGAL RESTRICTIONS FOR PUBLICATION OR PRESENTATION THROUGH A COLLABORATIVE RESEARCH AND DEVELOPMENT AGREEMENT (CRADA), MATERIAL TRANSFER AGREEMENT (MTA), INTELLECTUAL PROPERTY RIGHTS AGREEMENT ETC.?
☐ YES ☒ NO **NOTE:** If the answer is YES then attach a copy of the Agreement to the Publications/Presentations Request Form.

11. MATERIAL IS FOR: ☒ DOMESTIC RELEASE ☐ FOREIGN RELEASE
CHECK APPROPRIATE BOX OR BOXES FOR APPROVAL WITH THIS REQUEST. ATTACH COPY OF MATERIAL TO BE PUBLISHED/PRESENTED.

☐ 11a. PUBLICATION/JOURNAL (List intended publication/journal.)

☐ 11b. PUBLISHED ABSTRACT (List intended journal.)

☐ 11c. POSTER (To be demonstrated at meeting: name of meeting, city, state, and date of meeting.)

☒ 11d. PLATFORM PRESENTATION (At civilian institutions: name of meeting, state, and date of meting.)
American Medical Society for Sports Medicine, Texas, 16-20 April 2016

☐ 11e. OTHER (Describe: name of meeting, city, state, and date of meeting.)

12. EXPECTED DATE WHEN YOU WILL NEED THE CRD TO SUBMIT YOUR CLEARED PRESENTATION/PUBLICATION TO DTIC
NOTE: All publications/presentations are required to be placed in the Defense Technical Information Center (DTIC).

DATE	
April 13, 2016	

13. 59 MDW PRIMARY POINT OF CONTACT (Last Name, First Name, M.I., email)	14. DUTY PHONE/PAGER NUMBER
Nye, Nathaniel S. (nathaniel.nye.1@us.af.mil)	671-4087

15. AUTHORSHIP AND CO-AUTHOR(S) List in the order they will appear in the manuscript.

LAST NAME, FIRST NAME AND M.I.	GRADE/RANK	SQUADRON/GROUP/OFFICE SYMBOL	INSTITUTION (If not 59 MDW)
a. Primary/Corresponding Author Nye, Nathaniel S.	O-3	559 THLS/ 559 MDG/ SGOZ	
b. Pawlak, Mary T.	O-3	559 THLS/ 559 MDG/ SGOZ	
c. Covey, Carl J.	O-4		Nellis AFB
d. Webber, Bryant J.	O-3	559 THLS/ 559 MDG/ SGOZ	
e. Beutler, Anthony I.	O-5		USUHS
f. Boden, Barry P.	N/A		The Orthopaedic Center

I CERTIFY ANY HUMAN OR ANIMAL RESEARCH RELATED STUDIES WERE APPROVED AND PERFORMED IN STRICT ACCORDANCE WITH 32 CFR 219, AFMAN 40-401_IP, AND 59 MDWI 41-108. I HAVE READ THE FINAL VERSION OF THE ATTACHED MATERIAL AND CERTIFY THAT IT IS AN ACCURATE MANUSCRIPT FOR PUBLICATION AND/OR PRESENTATION.

16. AUTHOR'S PRINTED NAME, RANK, GRADE	17. AUTHOR'S SIGNATURE	18. DATE
Nathaniel Nye, Capt, O-3	NYE.NATHANIEL.S.1244111692 Digitally signed by NYE.NATHANIEL.S.1244111692 Dn: c=US, o=U.S. Government, ou=DoD, ou=PKI, ou=USAF, cn=NYE.NATHANIEL.S.1244111692 Date: 2016.03.30 08:04:54 -05'00'	March 30, 2016
19. APPROVING AUTHORITY'S PRINTED NAME, RANK, TITLE	20. APPROVING AUTHORITY'S SIGNATURE	21. DATE
Asha Mandhare, Maj, 559 THS Flight Commander	MANDHARE.ASHA.K.1120419753 Digitally signed by MANDHARE.ASHA.K.1120419753 Dn: c=US, o=U.S. Government, ou=DoD, ou=PKI, ou=USAF, cn=MANDHARE.ASHA.K.1120419753 Date: 2016.03.30 12:08:30 -05'00'	March 30, 2016

PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

1st ENDORSEMENT (59 MDW/SGVU Use Only)

TO: Clinical Research Division 59 MDW/CRD Contact 292-7141 for email instructions.	22. DATE RECEIVED 30 Mar 2016	23. ASSIGNED PROCESSING REQUEST FILE NUMBER 16150

24. DATE REVIEWED	25. DATE FORWARDED TO 502 ISG/JAC
31 Mar 2016	

26. AUTHOR CONTACTED FOR RECOMMENDED OR NECESSARY CHANGES: ☒ NO ☐ YES If yes, give date. _____ ☐ N/A

27. COMMENTS ☒ APPROVED ☐ DISAPPROVED

The presentation is approved.

28. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER	29. REVIEWER SIGNATURE	30. DATE
Rocky Calcote, PhD, Clinical Research Administrator	CALCOTE.ROCKY.D.1178245844 Digitally signed by CALCOTE.ROCKY.D.1178245844 DN: c=US, o=U.S. Government, ou=DoD, ou=PKI, ou=USAF, cn=CALCOTE.ROCKY.D.1178245844 Date: 2016.03.31 09:23:56 -05'00'	

2nd ENDORSEMENT (502 ISG/JAC Use Only)

31. DATE RECEIVED	32. DATE FORWARDED TO 59 MDW/PA

33. COMMENTS ☐ APPROVED (In compliance with security and policy review directives.) ☐ DISAPPROVED

34. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER	35. REVIEWER SIGNATURE	36. DATE

3rd ENDORSEMENT (59 MDW/PA Use Only)

37. DATE RECEIVED	38. DATE FORWARDED TO 59 MDW/SGVU
April 15, 2016	April 15, 2016

39. COMMENTS ☒ APPROVED (In compliance with security and policy review directives.) ☐ DISAPPROVED

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"The views expressed are those of the [author(s)] [presenter(s)] and do not reflect the official views or policy of the Department of Defense or its Components"

40. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER	41. REVIEWER SIGNATURE	42. DATE
Kevin Iinuma, SSgt/E-5, 59 MDW Public Affairs	IINUMA.KEVIN.MITSUGU.1296227613 Digitally signed by IINUMA.KEVIN.MITSUGU.1296227613 DN: c=US, o=U.S. Government, ou=DoD, ou=PKI, ou=USAF, cn=IINUMA.KEVIN.MITSUGU.1296227613 Date: 2016.04.15 10:34:56 -05'00'	April 15, 2016

4th ENDORSEMENT (59 MDW/SGVU Use Only)

43. DATE RECEIVED	44. SENIOR AUTHOR NOTIFIED BY PHONE OF APPROVAL OR DISAPPROVAL ☐ YES ☐ NO ☐ COULD NOT BE REACHED ☐ LEFT MESSAGE

45. COMMENTS ☐ APPROVED ☐ DISAPPROVED

46. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER	47. REVIEWER SIGNATURE	48. DATE

Strengthening the Foundation of Warrior Health

IMPROVING STRESS FRACTURE DIAGNOSIS: Algorithm and Clinical Prediction Rule

Nye NS,[1] Pawlak MT,[1] Covey CJ,[2] Webber BJ,[1] Beutler AI,[2] Boden BP[3]

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[3]The Orthopaedic Center, Rockville, MD 20850

Keep the Pipeline Flowing

Disclaimer

- No financial relationships
- The views expressed are those of the authors and do not reflect the official views or policy of the Department of Defense or its Components

Stress Fractures in Air Force BMT

Strengthening the Foundation of Warrior Health

- FY2012-2014: 1,218 stress fx
  - Approximately 400 cases per year
- FY14:
  - 459 Stress fractures
  - 414 had a bone scan
    - Only 25 had MRI
  - 1071 bone scans ordered → 38.7% positive rate
  - Of 414 positive bone scans:
    - 5.8% were negative in symptomatic location, but positive in asymptomatic location
    - 21% of MRI's performed average of 6 days later were negative

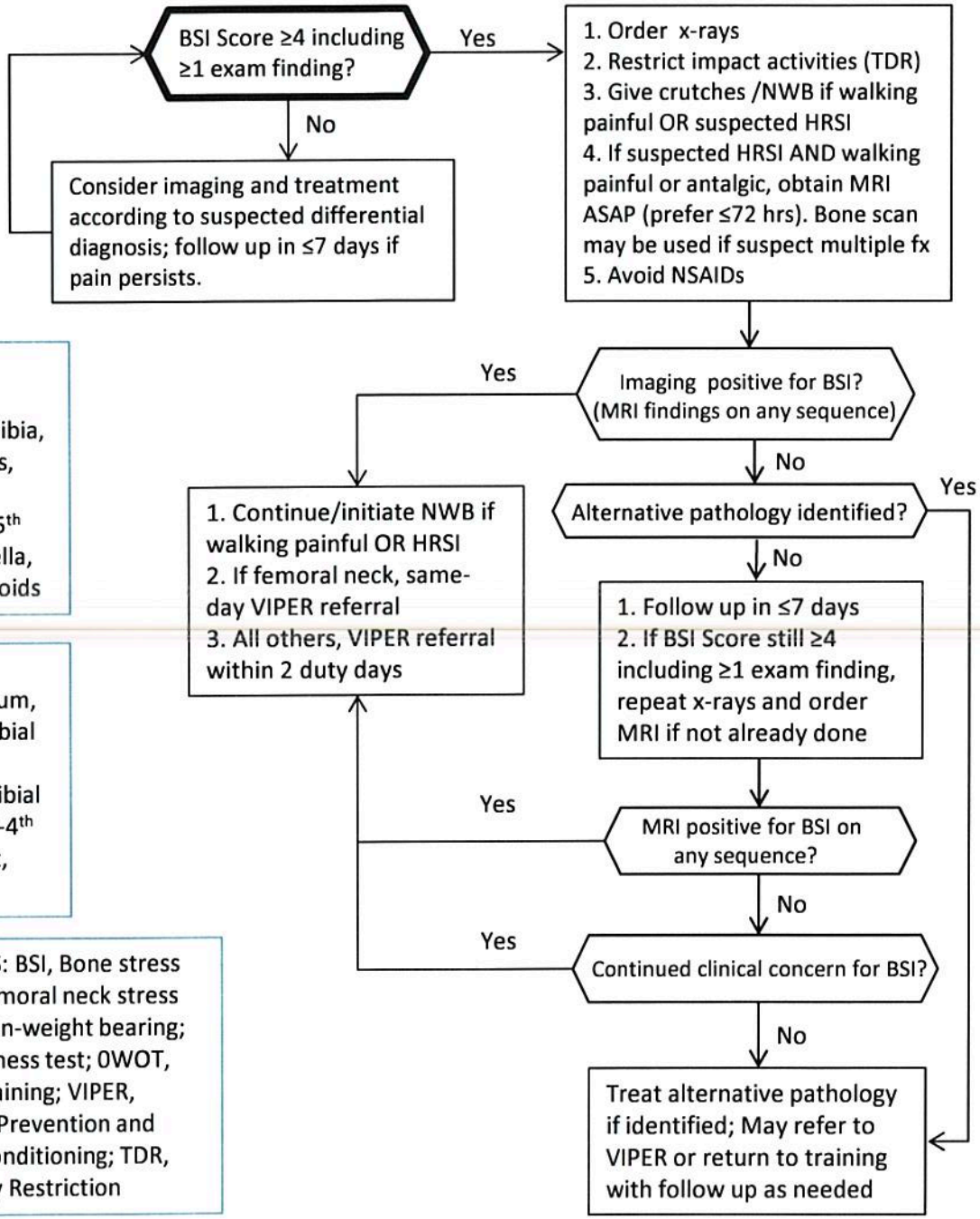
Developed Algorithm & CPR

- ACR: x-rays indicated as first line imaging in all cases
- MRI more sensitive and specific than bone scan
- Developed threshold to begin a workup
- Incorporates 1 wk of "triage by time" before advanced imaging

- Nye NS, Covey CJ, Sheldon LM, Webber BJ, Pawlak MT, Boden BP, Beutler AI. Improving diagnostic accuracy and efficiency of suspected bone stress injuries: algorithm and clinical prediction rule. *Sports Health*. 2016 Mar 4 [epub ahead of print]

Sports Health
A Multidisciplinary Approach

Diagnosis and initial management of bone stress injury (BSI) in Trainee Health



High risk:
Femoral neck, anterior cortex tibia, medial malleolus, navicular, talus, proximal 2nd or 5th metatarsal, patella, great toe sesamoids

Low risk:
Pubic rami, sacrum, femoral shaft, tibial plateau, posteromedial tibial shaft, fibula, 2nd-4th metatarsal shaft, calcaneus

ABBREVIATIONS: BSI, Bone stress injury; HRSI, Femoral neck stress injury; NWB, Non-weight bearing; PFT, Physical fitness test; 0WOT, Zero week of training; VIPER, Versatile Injury Prevention and Embedded Reconditioning; TDR, Temporary Duty Restriction

BSI SCORE:

Risk Factors (1 pt each):
- Poor baseline aerobic fitness (>14:00 on 0WOT 1.5-mile run)
- Female gender
- ≥2 missed periods in last 6 months
- Prior stress fracture
- Known vitamin D deficiency
- Eating disorder or caloric insufficiency
- Pes cavus (high arches)

Symptoms (1 pt each):
- Gradual onset pain (atraumatic)
- Pain worsens during activity
- Mostly dull, aching pain
- Recent increase in activity
- Night pain

Exam (1 pt each):
- Bone focally tender to palpation
- Pain with hip int. rotation (suspected femoral neck injury)
- Painful hop test (caution if suspected fem. neck stress injury)
- Painful fulcrum test
- Painful tuning fork test
- Antalgic gait

Diagnosis and initial management of bone stress injury (BSI) in Trainee Health

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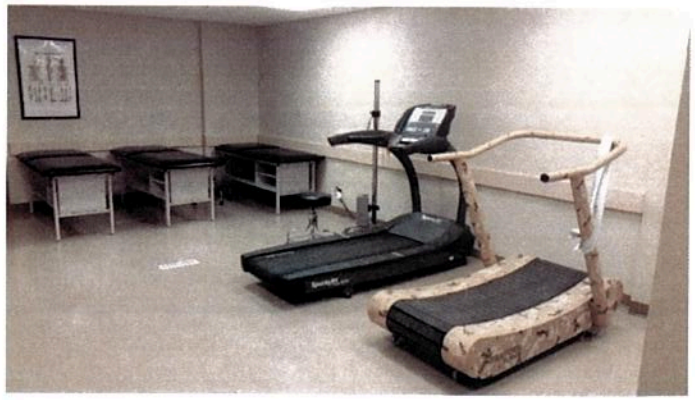
Validating clinical prediction rule: Methods

- Enrolled 527 patients with lower extremity pain between 15 July 2015 – 29 Mar 2016
- All patients evaluated with BSI score
- Outcome of interest: ICD-10 code for stress fx
  - >30 days follow up
- A BSI score ≥4 with ≥1 positive physical exam finding established the threshold to begin diagnostic evaluation and activity restriction
- Test characteristics for various BSI score cutoffs were calculated



Results

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- 132 diagnosed with a stress fracture
- BSI score cutoff of ≥4+PE yielded
  - 84.9% sensitivity (95% CI: 77.3-90.3)
  - 43.0% specificity (95%CI 38.1-48.1)
  - 89.5% negative predictive value (NPV) (95% CI: 84.0-93.3)
  - 1.49 positive likelihood ratio (LR+) (95% CI: 1.33-1.67)
- A BSI score cutoff of ≥3+PE did not increase NPV
- A BSI score of ≥7+PE was more specific (78.5%, 95% CI: 74.0-82.4) and had LR+ of 2.28 (95% CI: 1.77-2.96).

Frequency of bone stress injury score in USAF recruits with and without stress fracture diagnosis

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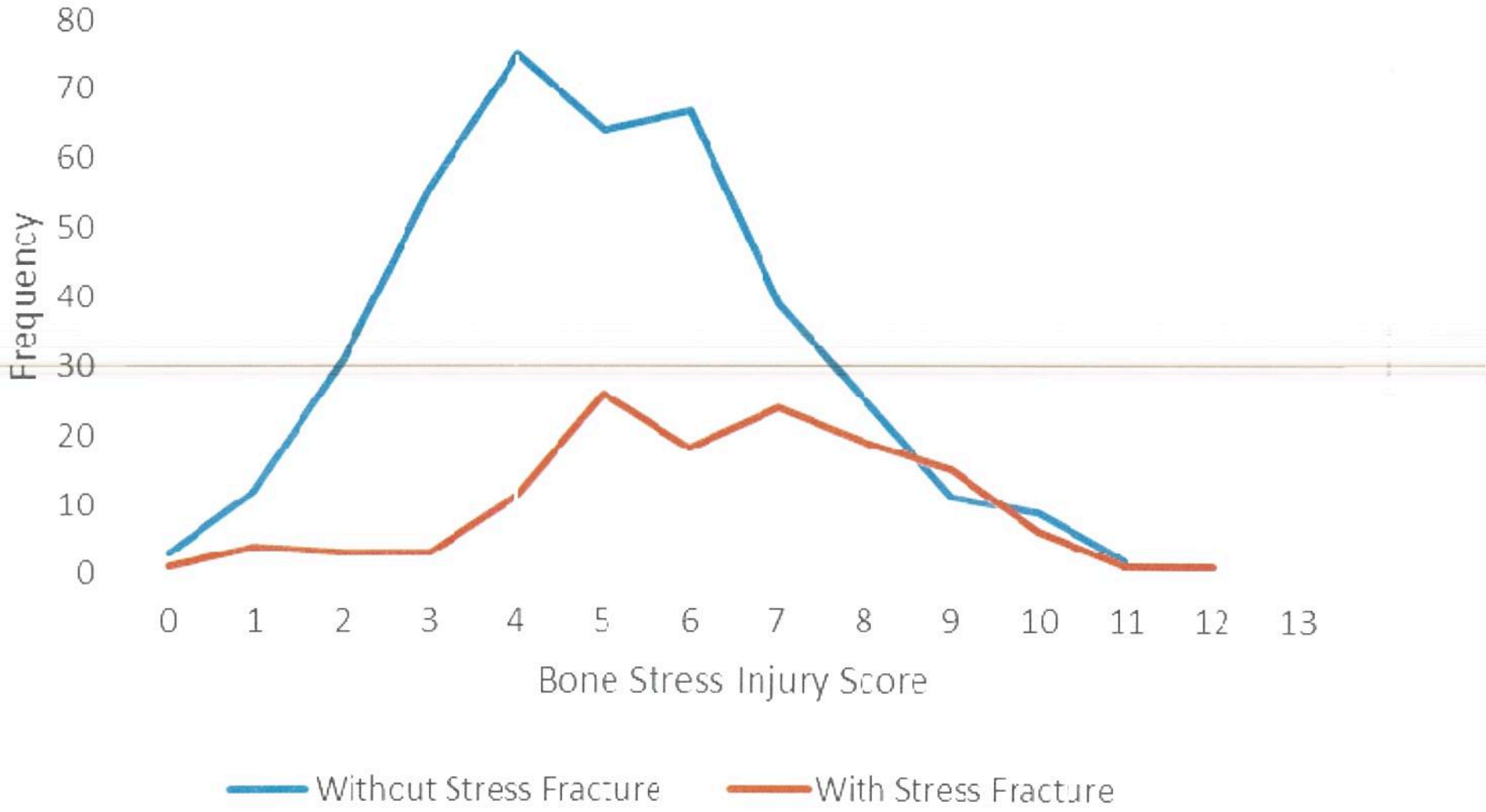

Validation of bone stress injury score to predict clinical diagnosis of stress fracture

Strengthening the Foundation of Warrior Health

BSI score cut-off (% at or above cut-off)	Sensitivity, %	Specificity, %	PPV, %	NPV, %	LL+	LL-
BSI ≥3 and positive physical exam (68)	86	38	32	89	1.4	0.37
BSI ≥4 and positive physical exam (64)	85	43	33	89	1.5	0.35
BSI ≥5 and positive physical exam (55)	79	53	36	88	1.7	0.4
BSI ≥6 and positive physical exam (42)	62	65	37	84	1.8	0.58
BSI ≥7 and positive physical exam (28)	49	78	43	82	2.2	0.65

Discussion

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- A score threshold of ≥4+PE provided an effective screen
- Subthreshold scores ruled out stress fractures quite accurately in this population
- A score of ≥7+PE showed utility for ruling in stress fracture.
- The algorithm and BSI score provide useful guides for clinical decision-making
- Do they reduce unnecessary testing or surveillance bias?

FY 2015: Impact of algorithm & CPR

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	FY 2014	FY 2015
Number of stress fracture	459	362
Bone scans ordered (% positive)	1071 (38.9)	86 (97.7)
Xray + bone scan	325	75
XRay + MRI	25	205
XRay + bone scan + MRI	85	18
XRay only	20	80

Fast MRI Protocol for Stress Fx

Strengthening the Foundation of Warrior Health

- SCREENING STUDY
- STIR & T1
- Both in 2 orthogonal planes
- Reduces scan time from 50-60 to 15 minutes
- Not recommended after another screening study (fast MRI, bone scan)

References

1. Nye NS, Covey CJ, Sheldon LM, Webber BJ, Pawlak MT, Boden BP, Beutler AI. Improving diagnostic accuracy and efficiency of suspected bone stress injuries: algorithm and clinical prediction rule. *Sports Health*. 2016 Mar 4 [epub ahead of print]
2. Kaeding CC, Miller T. The Comprehensive Description of Stress Fractures: A New Classification System. *J Bone Joint Surg Am.* 2013;95(13):1214-1220.
3. Jacobs JM, Cameron KL, Bojescul JA. Lower Extremity Stress Fractures in the Military. *Clin Sports Med.* 2014;33(4):591-613.
4. Wright AA, Hegedus EJ, Lenchik L, Kuhn KJ, Santiago L, Smoliga JM. Diagnostic Accuracy of Various Imaging Modalities for Suspected Lower Extremity Stress Fractures: A Systematic Review with Evidence-Based Recommendations for Clinical Practice. *Am J Sports Med.* 2015, Mar 24 Epub ahead of print.
5. Daffner RH, Weissner BN, Appel M, et al. ACR Appropriateness Criteria Stress (Fatigue/Insufficiency) Fracture, Including Sacrum, Excluding Other Vertebrae. 2011. Accessed Apr. 14, 2015 at: *http://www.guideline.gov/content.aspx?id=32618.*

Questions?

PROTOCOL FOR CLINICAL INVESTIGATION – EXEMPT
(Wilford Hall Ambulatory Surgical Center – WHASC)

1. Title:

Evaluating an Algorithm and Clinical Prediction Rule to Improve Diagnostic Accuracy and Management of Pelvic and Lower Extremity Bone Stress Injuries
FWH#:

2.0. Principal Investigator (PI): **WHASC PI:** **Co-PI:**

Name	Nathaniel Nye	Carlton Covey
Rank/Corps or Civilian Rating	Capt/MC	Maj/MC
Date of IRB Approved CITI Training	12/13/14	6/19/13
Branch of Service	USAF	USAF
AD Mil/DoD Civilian/Ctr/Non-DoD Civ	AD	AD
Department & Base	Trainee Health Surveillance, JBSA-Lackland	Family Medicine, Nellis AFB
Phone & Pager #	(614) 598-9258	(240) 447-4431
E-Mail Address	Nathaniel.nye.1@us.af.mil	Carlton.covey@us.af.mil

2.1. Associate Investigators (AIs): None

2.2. Research Assistants (RAs) & Coordinators (RCs):

Name	AD/DoD Civ/Ctr/ Non-DoD Civ	Rank/Corps or Civilian Rating/Title	Date of CITI Training	Phone & Pager #
Jill Clark, MBA/HCM, CCRC	CTR	Clinical Research Manager	03/20/14	(702) 653-3298

2.3. The research relevance of this protocol focuses on: [x] **Diagnosis** [x] **Treatment** [x] **Medical Utilization/Managed Care** [] **Prevention** [] **Medical Readiness** [] **Other**

2.4. Location(s):

a. Collaborating Facilities: N/A
b. Air Force Sites seeking Regional IRB: Jill Clark, (702) 653-3298
c. List study sponsors: N/A

3. Exempt Category: This protocol fits the following Exempt Category:

3.3. Category 32 CFR 219.101(b)(4): This research involves the collection or study of:

1) existing data,
2) existing documents,
3) existing records,

The information will be recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects (e.g., codes).

4.0. Research Plan:

4.1. Purpose: The purpose of this study is to validate a novel clinical prediction rule as part of a diagnostic and initial treatment algorithm for lower extremity stress injuries.

4.2. Hypotheses, Research Questions or Objectives: In patients that present with lower extremity pain, what bone stress injury (BSI) score range correlates with high risk (and low risk) for having a lower extremity stress injury? Our hypothesis is that a BSI score ≥4 (with ≥1 exam finding) will provide a satisfactory threshold for designation of low and high risk groups.

4.3. Significance: Stress fracture incidence among military recruits (43.8 per 1000 person-years) is 18 times higher than among active component service members (2.4 per 1,000 person-years). Lower extremity stress fractures significantly impair military readiness in terms of medical costs, lost training time, medical attrition during training, and early medical discharge. The total cost of all stress fractures in Air Force Basic Military Training in 2009 was over 4.8 million dollars. At this time there is no published clinical prediction rule for the diagnosis and initial management of bone stress injuries. The purpose of this study is to validate the clinical prediction rule as part of the diagnostic/treatment algorithm.

4.4. Military Relevance: A validated clinical prediction rule has the possibility decreasing unnecessary imaging, medical and nonmedical costs, attrition due to stress fracture, and time away from training. It also will help providers with less robust clinical musculoskeletal background to properly diagnose and initially manage patients with bone stress injuries.

4.5. Background and Review of Literature: Stress fractures are common among trainees and present a fiscal and readiness challenge in all branches of the U.S. military. The cumulative incidence of lower extremity stress fractures during entry-level military training ranges from 0.8% to 6.9% for males and 3.4% to 21.0% for females, with the tibia being the prominent site[2,4]. At Joint Base San Antonio-Lackland, site of all Basic Military Training, the incidence of stress fractures increased 56% from fiscal year 2012 to 2014. This led many of the providers in the Trainee Health Clinic to have an increased index of suspicion of stress fractures, which led to many bone scans being ordered to evaluate suspected stress injuries; even in patients that had low risk for stress injury. Many of the bone scans showed positive findings in asymptomatic areas needing further work up and time lost from training. This apparent surveillance bias and overdiagnosis rate associated with bone scans suggested the need for a standardized diagnostic algorithm that all Trainee Health Clinic providers can use. The initial part of any good algorithm is proper patient selection. At this time there is no clinical prediction rule in the literature for diagnosing significant bone stress injuries[3]. We developed the bone stress injury (BSI) score to help identify moderate to high-risk individuals to help expedite the workup of bone stress injury. The BSI, and corresponding algorithm, also will identify low risk individuals that may not need full radiographic workup and time away from training. Proper identification of each of these cohorts can help guide early and proper treatment for those who need it to prevent catastrophic injury as well as return all trainees to duty as soon as possible[5]. Models for predicting rehabilitation time and return date, which have been described in the context of collegiate and professional sports, would likely have a profound impact on military readiness if found to be applicable in military training environments[1,6]. Recent literature has confirmed that MRI is the most sensitive and specific modality to diagnose significant bone stress injuries[7]. Plain radiographs are highly specific (88-96%) but poorly sensitive (12-56%)[7]. Bone scans are highly sensitive but has limited specificity for stress fractures since tumor, infection, inflammation, or trauma can all cause increase in radiotracer uptake[7]. Many existing algorithms for evaluation and treatment of stress fractures do not contain clinical prediction rules and/or rely primarily upon bone scan[3]. This is the impetus for our initial study of choice (after plain radiographs) to be MRI to evaluate potential significant bone stress injury.

4.5.1. Bibliography:

1. Dobrindt O, Hoffmeyer B, Ruf J, et al. Estimation of return-to-sports-time for athletes with stress fracture-an approach combining risk level of fracture site with severity based on imaging. *BMC Musculoskeletal Disorders*. 2012;13:139.
2. Jacobs JM, Cameron KL, Bojescul JA. Lower extremity stress fractures in the military. *Clin Sports Med*. 2014;33(4):591-613.
3. Kaeding, C. C. and T. Miller. The comprehensive description of stress fractures: a new classification system. *J Bone Joint Surg Am* 2013;95(13): 1214-1220.
4. Knapik J, Montain SJ, McGraw S, et al. Stress fracture risk factors in basic combat training. *Int J Sports Med*. 2012;33(11):940-6.
5. Kupferer KR, Bush DM, Cornell JE, et al. Femoral neck stress fracture in Air Force basic trainees. *Mil Med*. Jan 2014;179(1):56-61.
6. Nattiv A, Kennedy G, Barrack MT, et al. Correlation of MRI grading of bone stress injuries with clinical risk factors and return to play: a 5-year prospective study in collegiate track and field athletes. *Am J Sports Med*. 2013;41(8):1930-41.
7. Wright AA, Hegedus EJ, Lenchik L, et al. Diagnostic accuracy of various imaging modalities for suspected lower extremity stress fractures: a systematic review with evidence-based recommendations for clinical practice. Am J Sports Med. 2015

4.6. Research Design and Methods: A total of 500 (250 male and 250 female) USAF basic military trainees and technical training students who have completed the BSI score will be selected. All data will be gathered and de-identified by Juste Tchandja, PhD, MPH, and sent to the Principal Investigators for analysis.

The care provided to patients enrolled and data collected for this study do not deviate from usual care/usual data collection according to written policy of the 559th Medical Group. The study design is a retrospective analysis of an existing data set. Because individuals become eligible for inclusion in the data set at the time of presentation for medical care, prospective cohort statistical measures will be employed for analysis.

Medical providers at the Trainee Health Clinic are intermittently given refresher training on the stress injury diagnostic algorithm (attachment 1), and reminded of the importance of completeness of records, accurate BSI score calculation, and precisely following the algorithm. They will be reminded that medical judgment cannot always be cleanly dictated by an algorithm, however, and that sound judgment may require deviation from the algorithm. Cases that deviated from the algorithm at the level of the clinical prediction rule will be excluded from the main analysis and analyzed separately.

Per written 559th policy, patients presenting to the Trainee Health Reid Clinic complaining of lower extremity pain are administered a simple questionnaire regarding BSI risk factors and symptoms by the medical technician (attachment 2). The provider reviews the questionnaire, obtains additional history and performs the appropriate physical exam, and then fills the patient's relevant findings into the template that is copied into AHLTA. This process was put into place early in 2015 in order to standardize the evaluation and workup of lower extremity pain among trainees.

Since 2013, a stress fracture registry has been maintained by the Trainee Health Surveillance Flight at JBSA-Lackland, in accordance with DoDD 6490.02E "Comprehensive Health Surveillance," AFI 48-105 "Surveillance, Prevention, and Control of Disease and Conditions of Public Health or Military Significance," and AETCI 48-103 "Training Health and Human Performance Program" (specifically para 3.5.3.2.1). The registry captures all basic military trainees and technical training students at JBSA-Lackland who are diagnosed with a stress fracture. This registry includes demographic data, date of diagnosis, imaging modalities used, location of symptoms, concordance/discordance of imaging with symptoms, presence of a fracture line, incidence of displaced fracture, cases referred to orthopedics, and cases requiring surgery.

4.6.1. Interventions, Observations, or Data Sought: Definition of the primary outcome of interest is any ICD-9-CM code for stress fracture or stress reaction of the lower extremity, to include pelvis and sacrum, but excluding lumbar spine, torso, and upper extremities. Incident cases identified will have charts reviewed (per routine procedure for stress fracture registry) by the research team for secondary outcomes of interest. These include the presence of a fracture line (as reported by radiologist on MRI or x-ray, excluding acute fractures), any displaced stress fracture reported by the radiologist, and attrition for stress fracture (verified through Basic Training Management System). Chart review will also verify that the imaging findings correlate with the location of the patient's symptoms. If the imaging findings are separated from the patient's symptoms by two or more long bones (i.e., femur and tibia, such as when symptoms are located in hip region but imaging positive in the ankle or foot) or are in the contralateral extremity, and the patient did not have symptoms or exam findings in the location indicated on imaging, then the imaging findings will be considered discordant and not counted as an outcome of interest.

To further clarify, the radiologist must report bone marrow edema on any sequence of the MRI to meet our definition of an outcome of interest; periosteal edema alone does not meet our definition of an outcome of interest. If the radiologist does not specify what findings he/she is considering a stress injury, the images will be reviewed by another radiologist to confirm whether bone marrow edema is present (in most cases, this will be Lt Col Sheldon). An outcome of interest also includes any focal uptake on bone scan which is described by the radiologist as a possible stress fracture, stress injury, or "stress change," not to include diffuse uptake described as "shin splints" or "thigh splints".

Patients who present to the clinic more than once with lower extremity pain will be administered a BSI questionnaire at each visit. For purposes of this investigation, their charts will be followed for 3 months from the time of their first encounter for lower extremity pain. For patients who have had multiple BSI scores calculated, we will use the most recent score prior to diagnosis for analysis.

4.6.2. Data Collection and Processing: A log will be kept by each medical technician including each patient who presents with lower extremity pain and is administered a BSI questionnaire. On a weekly basis, these logs will be turned into the Trainee Health Surveillance epidemiologist, Juste Tchandja, PhD, MPH, who maintains the stress fracture registry. At the conclusion of the study, all personally identifying information will be removed prior to sending to the Principal Investigators.

4.6.3. Setting: JBSA-Lackland, Texas

4.6.4. Date(s): July 2015 – July 2016

4.6.5. Source of Research Material:

Source of Research Material per Participant (Procedures)	# Routine Care	# Research Driven	# Total Procedures
Stress Fracture Registry	1	0	1

Only records or database entries in existence at the time of study approval will be examined in this study. All data will be recorded by the investigator in such a manner that subjects cannot be identified directly or through identifiers or codes linked to the subjects.

4.6.6. Subjects: Air Force basic military trainees and technical training students at JBSA-Lackland

4.6.7. Inclusion/Exclusion Criteria:
Inclusion: Air Force basic military trainees and technical training students at JBSA-Lackland who present to the Trainee Health Reid Clinic with lower extremity pain and who complete the BSI

Exclusion: No exclusion criteria will be applied. (Of note, all females are administered a pregnancy test upon arrival and all patients with positive pregnancy test are promptly discharged home for civilian medical care).

4.6.8. Instrumentation: N/A

5.0. Human Subject Protection:

5.1. Recruitment and Consent Processes: Approximately 500 (250 male and 250 female) trainees at JBSA-Lackland presenting to the Trainee Health Clinic with lower extremity pain will be selected from their existing medical record. All information obtained by the Principal Investigators will be de-identified. Informed Consent will not be sought from research participants because the research could not practicably be carried out if consent was obtained, waiver of consent would not adversely affect the rights and welfare of the subjects and the research involves no more than minimal risk to subjects.

5.2. Benefits: This study may have no direct benefit to participants, however it may benefit future military Trainees by preventing unnecessary radiographic imaging and allowing return to training faster, with or without a bone stress injury

5.3. Risks: There is a risk of inadvertent breach of confidentiality.

5.4. Safeguards for Protecting Information: Data collected will be de-identified prior to review and analysis by the investigator. It will be kept on a government computer assigned to the PI. The computer is password and CAC protected, and the system is firewall protected. There are no planned linkages with external databases, nor is transmission of the data for collaborative use anticipated. Following completion of the study the data will be stored and destroyed in compliance with policies implemented by the WHMC IRB.

6.1. Outcome Measures:

- Demographic data: age (at first encounter) and sex
- Independent variable: BSI score
- Primary dependent (outcome) variable: pelvic or lower extremity stress fracture within 3 months of initial BSI, as determined by ICD-9-CM codes of 733.14-.16, 733.93-94, or 733.96-98
- Secondary dependent (outcome) variables:
  1) Fracture line reported by radiologist on MRI or x-ray, excluding acute fractures
  2) Displaced stress fracture
  3) Attrition for stress fracture
- Potential confounding variables:
  1) Time from initial encounter to a primary and/or secondary outcome of interest
  2) Number of medical encounters for lower extremity pain (excluding administrative and physical therapy visits)

6.2. Sample size estimation/power analysis: We previously found that approximately 10% (565/5785) of trainees who presented to the Trainee Health Reid Clinic with lower extremity pain or inflammation over a two-year period were diagnosed with a stress injury (*J Athletic Training*, in press). We anticipate that trainees who present to clinic with lower extremity pain or inflammation and have a low BSI score (0-3 and any who lack exam findings) will have a lower rate of being diagnosed with stress injury (≤10%), whereas those with high scores (≥4 including ≥1 exam finding) will have a higher rate of being diagnosed with stress injury (≥25%). Assuming 1:1 ratio between those with "low" and "high" BSI scores, we would require 200 subjects to have 80% power to detect this 15% risk difference at the alpha = 0.05 level. It may be more likely, however, that more trainees will score in the "low" category. Assuming a 3:1 ratio between those with "low" and "high" BSI scores, we would require approximately 250 subjects (62 with low scores and 184 with high scores) to have 80% power to detect this 15% risk difference at the alpha = 0.05 level. We would also like to analyze the clinical prediction rule by sex, so we would like to have enough males and females to stratify by sex, so we will anticipate requiring 500 total subjects (250 males and 250 females) in order to have adequate power to analyze the BSI clinical prediction rule. If current rates of presentation continue, we anticipate having these numbers in 2-3 months.

6.3. Statistical Analysis: Distribution of BSI scores (frequency, one score per patient), and rate and relative risk of stress fracture diagnosis associated with each BSI score will be calculated. To determine the most appropriate number of points (weight) assigned to each element of the BSI score (each is a binary variable which indicates a clinical finding being either present or absent), beta coefficients for each variable in the score will be calculated. Variables with a significantly higher beta coefficient will be assigned 2 or more points, whereas if all variables have a similar beta coefficient (difference less than 5), all variables will be assigned one possible point. Receiver-operator characteristic (ROC) curves will be used to determine the BSI score which provides optimum sensitivity and specificity. Rates and relative risks of secondary outcomes associated with each BSI score will also be calculated. Again, we believe (based on expert opinion only) that a BSI score of ≥4, including ≥1 exam finding, will be the best cut point, and therefore the sample size calculation is based on this.

6.4 Number of Subjects:

Number of subjects planned for JBSA	Enrolled in Study	500	to result in	500	completing study

TOTAL NUMBER OF SUBJECTS (nation-wide/study-wide): 500

7. Duration of Study: Approximate duration of the study: *1 year*
8. Local and External Support Services: None
9. Intramural (GME) and Extramural Funding Support: None
10. Conflict of Interest: None

11. Medical Research Area for the Study:

[] Analytical Chemistry	[] Anatomy	[] Anesthesiology	[] Biochemistry
[] Cardiovascular Surgery	[] Cardiology	[] Cell Biology	[] Dentistry
[] Dermatology	[] Dietetics	[] Electrophysiology	[] Endocrinology
[] Emergency medicine	[] Gastroenterology	[] General Surgery	[] Hematology
[] Histology	[] Immunology/Allergy	[] Infectious Disease	[] Microbiology
[] Molecular Biology	[] Neonatology	[] Neurology	[] Neurosurgery
[] Nursing	[] OB/GYN	[] Occupational Medicine	[] Occupational Therapy
[] Oncology	[] Ophthalmology	[] Oral/Maxillofacial Surgery	[X] Orthopedics
[] Pathology	[] Pediatrics	[] Pharmacology	[] Physical Therapy
[] Mental Health	[X] Radiology/Imaging	[] Urology	[] Wellness
[] Other (state):			

12. Attachments:

1. BSI AHLTA Template
2. BSI Questionnaire
3. Stress Fracture Algorithm
4. Form F: Waiver of Informed Consent
5. Form I: De-identification certification
6. Form J: HIPAA Authorization Waiver
7. Form A: Signature Form